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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,157	10/13/2005	Patrick Trotter	101713-5027	6570

28977 7590 06/02/2009

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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
06/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,157	TROTTER ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18,19 and 22* is/are pending in the application.

4a) Of the above claim(s) *7-10 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,11,13-16,18-19,22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/30/09 has been entered.

Applicants amendments and arguments filed 3/30/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously, applicants elected Group VIII (claims 1-6,11,13-22) and the peptide species of SEQ ID NO:19 (Gly-Arg-Gly-Asp) and the agent species being an antimicrobial.

As discussed below, claims to the elected species are obviated based on the prior art. In accord with section 803.02 of the MPEP the claims have been examined with respect to the elected species and claims to non-elected species are withdrawn from consideration.

In the instant case, claims 7-10,12 are drawn to peptides other than the elected peptide.

Claims 7-10,12 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim.

Claims 17,20-21,23 have been cancelled.

Claims 1,6,11,15-16,18,22 have been amended.

Claims 1-6,11,13-16,18-19,22 are under consideration.

Claim Objections

Claims 1,11 are objected to because of the following informalities:

MPEP section 608.01(m) states that, "Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995)." However, claim 1 includes periods after I,II, and III. Periods should only be used at the end of the claim. It would be remedial to amend the claims to refer to 'I)' 'II)' and 'III)' for example.

Claim 11 lists the amino acid sequence -Gly-Arg-Gly-Asp-. However, the standard in the art (for example, see SEQ ID NO:2 of claim 7) is to use dashes (-) in between the amino acids and not at the beginning and end (i.e. Gly-Arg-Gly-Asp).

Appropriate correction is required.

Specification

It is noted that the PGPub for the instant application (US 20060269590) lists one of the inventors as 'Derrek Slloock'. However, application 10497442 (for which there was a double patenting rejection in the previous office action) and corresponding PGPub US 20050159695 lists 'Derek Silcock' as one of the inventors. As such, there is a reasonable basis that there may have been a typographical or transliteration error in the spelling of an inventors name.

Section 605.04b of the MPEP states:

"When a typographical or transliteration error in the spelling of an inventor's name is discovered during pendency of an application, a petition is not required, nor is a new oath or declaration under 37 CFR 1.63 needed. However, applicants are strongly encouraged

to use an application data sheet such that any patent to issue will reflect the correct spelling of the inventor's name. Without an application data sheet with the corrected spelling, any patent to issue is less likely to reflect the correct spelling since the spelling of the inventor's name is taken from the oath or declaration, or any subsequently filed application data sheet."

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6,13-16,18-19,22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 and dependent claims 3-6,13-16,18-19,22 refer to a 'protease associated with wound fluid' or a 'protease associated with wound infection or ulcer formation'. On page 4 lines 4-8 of the specification a 'protease associated with wound fluid' and a 'protease associated with wound infection or ulcer formation' are discussed. First, it is noted that wound infection or ulcer formation (as discussed on page 4 of the specification) is not necessarily the equivalent of wound fluid (as recited in claim 1). Further, exemplification is not a specific precise definition. In the instant case, page 4 provides examples (i.e. 'we include'). However, an example is not a definition. Further, the example for a 'protease associated with wound fluid' is in reference to 'wounds that are apparently not clinically infected'. It is unclear what falls within the scope of 'apparently not clinically infected' as such phrase appears to depend on ones subjective opinion.

The metes and bounds of a 'protease associated with wound fluid' is unclear. The word 'associated' as used in the instant claims can be interpreted in different fashions. For example, the term could mean that the wound fluid includes a protease or the term could mean that the presence of wound fluid triggers a cellular pathway to make the protease although the protease need not be present in the wound fluid. Further, the term could merely mean the wound fluid and a protease can be combined (i.e. associated).

Claim 3 refers to 'other factors'. The identity of the 'other factors' is unclear. The specification makes reference to proteases as factors (page 4 lines 28-29), however it is well-known in the art that growth factors are known to be present in bodily fluids. It is unclear if a growth factor would be within the scope of 'other factors'.

Claim 6 refers to 3 to 15 amino acids. It is unclear if the numbers are in reference to the length of the amino acid sequence or if the numbers are in reference to the types of amino acids present. For example, it is unclear if Lys-Lys-Lys would be considered to comprise 3 amino acids. Lys-Lys-Lys is 3 amino acids in length but comprises only the amino acid Lysine.

The term "substantially" in claim 18 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims were previously rejected under 112 1st written description. This rejection has been updated based on applicants amendments.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6,13-16,18-19,22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been

placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Further, to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include: a) the scope of the invention; b) actual reduction to practice; c) disclosure of drawings or structural chemical formulas; d) relevant identifying characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function correlation; e) method of making the claimed compounds; f) level of skill and knowledge in the art; and g) predictability in the art.

In the instant case, the claims are drawn to wound dressing compositions. Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any protease can be 'associated' with wound fluid as currently interpreted. The 'other factors' of claim 3 have been interpreted as any type of factor (i.e. a protease or growth factor, for example). Claim 6 has been interpreted as referring to a length of 3 to 15 amino acids. The term 'substantially' has been given the broadest reasonable interpretation such that any blockage or partial blockage is substantial.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high.

(2) Partial structure:

The claims are drawn to a wound dressing comprising oligopeptide sequences cleavable by a protease. Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any

protease can be 'associated' with wound fluid as currently interpreted. The 'other factors' of claim 3 have been interpreted as any type of factor (i.e. a protease or growth factor, for example). Claim 6 has been interpreted as referring to a length of 3 to 15 amino acids. The term 'substantially' has been given the broadest reasonable interpretation such that any blockage or partial blockage is substantial.

The oligopeptide sequences are described as being cleavable by a protease. The claims (such as claim 11) give examples of several oligopeptide sequences. However, nearly every protein is cleavable by a protease. For example, Matthews (Biochemistry 1996 as cited previously) teach numerous proteases such as trypsin, pepsin thrombin, and papain that would cleave an oligopeptide sequence. For example trypsin cleaves when R1 is Lys or Arg (see Table 5.4 of Matthews). If one considered a 10 amino acid peptide (R1-R10) oligomer with either Lys or Arg at R1 and any other amino acid except proline at R2 and any amino acid at the other positions there would be at least 20^8 (over 2 billion) possible peptides. Even though approximately 30 different oligopeptide sequences are recited in the specification, the recited peptides do not represent the genus. One of skill in the art would not recognize that the applicant was in possession of wound dressings with oligopeptide sequences of the scope of the genus of claims 1 and 23 for example.

The dressing is described as a matrix comprising polymers and a therapeutic agent. The specification (page 5) provides examples of numerous polymers. Claim 5 is drawn to a specific polymer. Claim 3 is drawn to polymers that are not degraded by protease or other factors. However, no examples are provided of a matrix comprising polymers and a therapeutic agent. An example appears on page 9 lines 19-25 which recite specific oligopeptide sequences and a

specific polymer. This example does not represent the claimed invention because the example does not recite a therapeutic agent. Therapeutic agents are a component of the wound dressing. The agents can be a variety of things (claim 13, page 10). However, no specific examples of wound dressings are provided. Although examples have been provided of components of the wound dressing no examples have been provided of a wound dressing as claimed. The example on page 9 lines 19-25 does not recite any agent.

There is substantial variability in the genus. Since there are a substantial variety of polypeptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The oligopeptide sequences are described as being cleavable by a protease. In particular the protease is described as being associated with would fluid, (claim 1,23 for example) wound infection or ulcer formation (claim 2). Claims 1,23 recite that the wound dressing is such that the rate of release of the therapeutic agent increases in the presence of the protease. However, there is no correlation provided between structure and function. No common structural attributes identify the members of the genus, in particular the oligopeptide sequences. For example, the recitation of 'associated with wound healing' does not lead one to particular wound dressing compositions or specific oligopeptide sequences. From the phrase 'rate of release of the therapeutic agent increases in the presence of the protease', one of skill in the art would not conclude any structural information. No common core sequence is taught for all the possible alternatives. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species or sufficient relevant identifying characteristics.

Regarding the polymer it is noted that claim 3 is drawn to polymers that are not degraded by protease or other factors. However, there is no correlation provided between structure and function. No common structural attributes identify the members of the genus, in particular the polymers that are not degraded by protease or other factors. From the phrase 'are not degraded by the protease or other factors', one of skill in the art would not conclude any structural information. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species or sufficient relevant identifying characteristics.

(5) Method of making the claimed invention:

The specification does not describe any specific embodiments of wound dressings nor methods of making them.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-6,13-16,18-19,22 are broad and generic, with respect to all possible wound dressings encompassed by the claims. The possible structural variations are limitless to any agent, polymer, and peptide meeting the claim limitations. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the components beyond those components specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of polypeptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of wound dressings embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and

does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments Written Description

Applicants argue that the group of proteases associated with wound fluid are known in the art and a reference (WO 00/64486) has been incorporated by reference. Applicants argue that the claims are to specific proteases. Applicants argue that examples are not necessary.

Applicant's arguments filed 3/30/09 have been fully considered but they are not persuasive.

Although applicants argue that a particular reference has been incorporated by reference, 37 CFR 1.57(b) states that that an incorporation must be express, clear, and clearly identify the reference. Further, MPEP section 601 states:

"Mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). >37 CFR 1.57(b)(1) limits a proper incorporation by reference (except as provided in 37 CFR 1.57(a)) to instances only where the perfecting words "incorporated by reference" or the root of the words "incorporate" (e.g., incorporating, incorporated) and "reference" (e.g., referencing) appear. The requirement for specific root words will bring greater clarity to the record and provide a bright line test as to where something is being referred to is an incorporation by reference. The Office intends to treat references to documents that do not meet this "bright line" test as noncompliant incorporations by reference and may require correction pursuant to 37

CFR 1.57(g). If a reference to a document does not clearly indicate an intended incorporation by reference, examination will proceed as if no incorporation by reference statement has been made and the Office will not expend resources trying to determine if an incorporation by reference was intended.< In addition to other requirements for an application, the referencing application *>must< include an identification of the referenced patent, application, or publication. >See 37 CFR 1.57(b)(2)"

In the instant case, Page 8 line 12 refers to WO 00/64486. However, the words 'incorporate' and/or 'reference' are not used on page 8. Although page 1 uses a generic incorporation statement, such statement does not clearly identify the specific subject matter to be incorporated. Further, 37 CRF 1.57(c) states that essential material may be incorporated by way of reference to a US Patent or US patent application publication which patent or patent application publication does not itself incorporate such essential material by reference. In the instant case, WO 00/64486 is not a US Patent or US patent application publication. As such, the instant specification does not provide adequate written description for the claimed invention.

Although Applicants argue that the claims are to specific proteases, although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any protease can be 'associated' with wound fluid as currently interpreted.

Although Applicants argue that examples are not necessary, examples are one of numerous factors to consider (see MPEP section 2163). In the instant case, 5 different factors are discussed above.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6,11,13-14,18-19,22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 (and dependent claims 2-6,11,13-14,18-19,22) refer to a wound dressing comprising 3 layers (wound contacting layer, intermediate layer, and outer backing layer) where at least one of the layers comprises a donor layer and barrier layer.

Claim 22 depends from claim 1 are refers to an additional backing layer.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any protease can be 'associated' with wound fluid as currently interpreted. The 'other factors' of claim 3 have been interpreted as any type of factor (i.e. a protease or growth factor, for example). Claim 6 has been interpreted as referring to a length of 3 to 15 amino acids. The term 'substantially' has been given the broadest reasonable interpretation such that any blockage or partial blockage is substantial.

Lack of Ipsis Verbis Support

The specification is void of any literal support for an outer backing layer that comprises a donor layer and barrier layer.

The specification is void of any literal support for multiple backing layers.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

The specification (original claims 15-16, specification page 11 lines 8-15) supports that the contacting layer or intermediate layer can comprise the matrix. However, the instant claims state that at least one of the layers (which includes the backing layer) comprises the matrix. The specification does not support that the backing layer comprises a donor layer and barrier layer or matrix. A discussion of the contacting or intermediate layer comprising the matrix would not lead one to recognize that the backing layer comprises the matrix. Hence, it can not be said that the specification provides support for at least one of said layers comprising the matrix.

The specification (original claim 22, page 14 lines 8-12) supports a backing layer. However, instant claim 22 is drawn to include multiple backing layers. The specification does not support the use of multiple backing layers. A discussion of a backing layer would not lead one to recognize that multiple backing layers are envisaged. Hence, it can not be said that the specification provides support for additional backing layers.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4,6,13-16,18-19,22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peppas et al (European Journal of Pharmaceutics and Biopharmaceutics 2000, 50:27-46) and Suzuki et al (J Biomed Mater Res 1998, 42:112-116) and Arnold (EP 0599589 as cited in IDS).

Peppas teach that hydrogels have numerous applications (abstract). Peppas teach that stimuli-sensitive hydrogel drug delivery systems are known in the art (page 34). Peppas specifically teach that Suzuki and associates prepared a PVA-based hydrogel with specially designed thrombin sensitive linkers (page 34-35 connecting paragraph). Peppas teach that antibiotics are released from the hydrogel only in the presence of infection (page 34-35

connecting paragraph). Peppas teach that the hydrogel can be used for a wound dressing with microbial infection-responsive controlled release antibiotics (page 34-35 connecting paragraph).

Peppas does not specifically teach a wound dressing with the components (in particular the layers) of the instant invention.

Since Peppas refers to the work of Suzuki and associates (page 34 last paragraph and reference 104) and suggest the use as a wound dressing (page 35) one would be motivated to use the information of the Suzuki reference. Suzuki teach a need for wound dressings with antibiotic release stimulated by microbial infection (page 112). Suzuki teach a PVA-(linker)-GM (where PVA is polyvinyl alcohol derivative and GM is gentamicin) delivery system (page 113 and Figure 1). Suzuki teach that various peptide linkers were tested in the presence of thrombin (table I). Suzuki teach that PVA-(linker)-GM showed selective release of gentamicin in wound fluid (page 115) and teach that the system could be applicable to numerous wound dressing applications (page 115 last paragraph).

Since both Peppas (page 35) and Suzuki (page 115) teach the use of the PVA-(linker)-GM as a wound dressing one would be motivated to formulate the system for wound dressing. Arnold teach wound dressings which are well known in the art (sections 0002-0010) and teach that a particular multi-layer wound dressing has been developed that has the advantages of the prior art and provides for improved wound healing (section 0011). Arnold specifically teach a wound dressing (section 0012, claims, Figure 1) that comprises a liquid permeable wound contacting layer, an intermediate layer and a outer protective layer that is impermeable to liquids (section 0022). Arnold teach the presence of a wound healing agent in one of the layers (section

0012). Arnold teach the presence of an absorbent layer to absorb wound exudate (section 0021). Arnold teach that the wound contacting layer may include compounds to assist wound healing (section 0027-0028). Arnold teach that the dressing inner layer has a particular pore size (section 0012).

Taken together, since both Peppas (page 35) and Suzuki (page 115) teach the use of the PVA-(linker)-GM as a wound dressing one would be motivated to formulate the system as a wound dressing using the wound dressing as taught by Arnold since Arnold teach a particular wound dressing that has the advantages of the prior art and provides for improved wound healing (section 0011). In particular, one would be motivated to use the PVA-(linker)-GM system of Suzuki in the wound dressing of Arnold. Since Suzuki teach PVA (polyvinyl alcohol derivative) the polymer limitations of claim 1 and 4 are met. Since Suzuki teach specific thrombin sensitive peptides (Table I) the peptide limitations of claims 1,6 are met. Since Suzuki teach GM (gentamicin) the limitations of claim 13 are met. In figure 1 of Suzuki the configuration of the system is shown. It is noted that the instant claims refer to cross-linkages. Since Figure 1 of Suzuki shows multiple monomeric units cross-linked together the system includes a matrix of cross-linked monomers. Further, since the peptide is part of the monomeric unit the cross-links comprise oligopeptide sequences as recited in claim 1. Since Suzuki teach that the peptides are thrombin sensitive the peptides are cleavable by a protease as recited in claims 1-2. Since Suzuki teach that the gentamicin is released and there is no evidence of degradation of the polymers the limitations of claim 3 are met absence evidence to the contrary. Based on Figure 1 of Suzuki it is shown that the gentamicin is in a donor layer and within a matrix and behind the barrier layer as recited in claims 1,14,18,22. It is noted that claim 19 provides no frame of reference with respect

to the orientation of behind. From figure 1 of Suzuki it is clear that at least one molecule of gentamicin would be behind the barrier layer. With respect to the layers, Arnold teach (section 0012, claims, Figure 1) layers I,II, and III as in the instant claims. Since Arnold teach the presence of a wound healing agent in one of the layers (section 0012) one would be motivated to incorporate the PVA-(linker)-GM system of Suzuki thus meeting the limitations of claim 1 of the instant invention. Since Arnold teach the presence of an absorbent layer to absorb wound exudate (section 0021) one would be motivated to include such layer thus meeting the limitations of claim 22. Since Arnold teach a outer protective layer that is impermeable to liquids (section 0022) any apertures would be substantially blocked as recited in claim 18. Since Arnold teach that the wound contacting layer may include compounds to assist wound healing (section 0027-0028) one would be motivated to include the PVA-(linker)-GM system in the wound contacting layer as recited in claims 14-15. Since Arnold teach that the intermediate layer may comprise a wound healing agent (section 0012) one would be motivated to include the PVA-(linker)-GM system on the wound contacting layer as recited in claims 14,16.

In the instant case, both Peppas and Suzuki set forth a specific antibiotic drug delivery system and motivate applications for wound healing. Since Arnold teach a particular wound dressing that has the advantages of the prior art and provides for improved wound healing (section 0011) one would be motivated to use the specific components of the dressing of Arnold. Since Suzuki teach that PVA-(linker)-GM showed selective release of gentamicin in wound fluid (page 115) and teach that the system could be applicable to numerous wound dressing applications (page 115 last paragraph) and Arnold teach a particular wound dressing that has the

advantages of the prior art and provides for improved wound healing (section 0011) one would have a reasonable expectation of success.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any protease can be 'associated' with wound fluid as currently interpreted. The 'other factors' of claim 3 have been interpreted as any type of factor (i.e. a protease or growth factor, for example). Claim 6 has been interpreted as referring to a length of 3 to 15 amino acids. The term 'substantially' has been given the broadest reasonable interpretation such that any blockage or partial blockage is substantial.

Claims 1-4,6,13-16,18-19,22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peppas et al (European Journal of Pharmaceutics and Biopharmaceutics 2000, 50:27-46) and Suzuki et al (J Biomed Mater Res 1998, 42:112-116) and Arnold (EP 0599589 as cited in IDS) and Ulbrich et al (Journal of Controlled Release 2000, 64:63-70 as cited in IDS).

As discussed above, Peppas and Suzuki and Arnold obviate claims 1-4.6,13-16,18-19,22.

The references do not teach in a single embodiment the polymer of claim 5.

Peppas teach (Table 1) a variety of monomers that are known to be used for pharmaceutical applications including VA and HPMA. Peppas teach that the chemical nature of the group used controls the properties and a number of monomers have been prepared with desired properties (page 28 section 2.1). Ulbrich specifically the use of HPMA conjugates

(abstract). Ulbrich teach that the HPMA backbone is modified by biodegradable peptide side chains (page 64 1st column) and teach that conjugates provided promising data in tests (page 78). Since Peppas teach that certain monomers have desired properties one would be motivated to substitute the PVA as taught by Suzuki with the HPMA as taught by Peppas and Ulbrich. The resulting systems would include the specific polymer recited in claim 5 of the instant invention.

The instant claims would have been obvious because the substitution of one known element (HPMA) for another (PVA) would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any protease can be 'associated' with wound fluid as currently interpreted. The 'other factors' of claim 3 have been interpreted as any type of factor (i.e. a protease or growth factor, for example). Claim 6 has been interpreted as referring to a length of 3 to 15 amino acids. The term 'substantially' has been given the broadest reasonable interpretation such that any blockage or partial blockage is substantial.

Claims 1-6,11,13-16,18-19,22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peppas et al (European Journal of Pharmaceutics and Biopharmaceutics 2000, 50:27-46) and Suzuki et al (J Biomed Mater Res 1998, 42:112-116) and Arnold (EP 0599589 as cited in IDS) and Ulbrich et al (Journal of controlled Release 2000, 64:63-70 as cited in IDS) and Pachence et al (WO 00/64486 as cited in IDS).

As discussed above, Peppas and Suzuki, Arnold, Ulbrich obviate claims 1-6,13-16,18-19,22.

The references do not specifically teach the peptides of claim 11.

Peppas recognizes (page 34) and Suzuki teaches (Table I) specific thrombin sensitive linkers. In fact, Suzuki tests various thrombin linkers (Table I) and reports various cleavage ratios for the linkers. Pachence teach Gly-Arg-Gly-Asp as a thrombin cleavage site (claims 28-29, page 16, lines 24-26, page 37 lines 9-14). Since Suzuki teach various linkers one would be motivated to test and use known linkers including the Gly-Arg-Gly-Asp as taught by Pachence to determine linkers with optimal cleavage ratios. When substituting the Gly-Arg-Gly-Asp for the peptide of Suzuki the resulting system obviates claim 11 of the instant invention.

The instant claims would have been obvious because the substitution of one known element (thrombin cleavage sites taught by Pachence) for another (thrombin cleavage sites taught by Suzuki) would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any protease can be 'associated' with wound fluid as currently interpreted. The 'other factors' of claim 3 have been interpreted as any type of factor (i.e. a protease or growth factor, for example). Claim 6 has been interpreted as referring to a length of 3 to 15 amino acids. The term 'substantially' has been

given the broadest reasonable interpretation such that any blockage or partial blockage is substantial.

Double Patenting

The terminal disclaimer filed on 3/30/09 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application Number 10/529,156 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 3/30/09 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application Number 10/497,442 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 3/30/09 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 7,361,634 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 3/30/09 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application Number 10/579,897 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6,13-16,18-19,22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4,7-16 of copending Application No. 12/041,955 ('955) in view of Arnold (EP 0599589 as cited in IDS).

'955 teach wound dressings comprising HPMA (claim 4) and specific peptide sequences cleavable by a protease (claim 1). Since HPMA is taught the polymer limitations of claims 4-5 are met. '955 reach that the polymers are not degraded (claim 2) as recited in claim 3. '955 teach antimicrobials (claim 7) as in claim 13 of the instant invention. '955 teach apertures (claim 12) as in claim 18 of the instant invention. '955 teach an absorbent layer (claim 16) as in claim 22 of the instant invention. '955 teach various layers and configurations (claims 9-10).

'955 does not teach all of the layers as in the instant claims.

Since '955 teach wound dressings one would be motivated to make specific wound dressings.

Arnold teach wound dressings which are well known in the art (sections 0002-0010) and teach that a particular wound dressing has been developed that has the advantages of the prior art and provides for improved wound healing (section 0011). Arnold specifically teach a wound dressing (section 0012, claims, Figure 1) that comprises a liquid permeable wound contacting layer, an intermediate layer and a outer protective layer that is impermeable to liquids (section 0022). Arnold teach the presence of a wound healing agent in one of the layers (section 0012). Arnold teach the presence of an absorbent layer to absorb wound exudate (section 0021). Arnold teach that the wound contacting layer may include compounds to assist wound healing (section 0027-0028). Arnold teach that the dressing inner layer has a particular pore size (section 0012).

Taken together, since '955 teach the use of specific structures as a wound dressing one would be motivated to formulate the system as a wound dressing using the wound dressing as taught by Arnold since Arnold teach a particular wound dressing that has the advantages of the prior art and provides for improved wound healing (section 0011). Since '955 teach HPMA the polymer limitations of claims 1,4-5 are met. '955 teach specific peptides the peptide limitations of claims 1,6 are met. Since '955 teach antibiotics the limitations of claim 13 are met. With respect to the layers, Arnold teach (section 0012, claims, Figure 1) layers I,II, and III as in the instant claims. Since Arnold teach that the presence of a wound healing agent in one of the layers (section 0012) one would be motivated to incorporate structure of '955 thus meeting the limitations of claim 1 of the instant invention.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP 2111). Since a protease can be recombinantly made and mixed with or combined with (i.e. associated) wound fluid, any protease can be

'associated' with wound fluid as currently interpreted. The 'other factors' of claim 3 have been interpreted as any type of factor (i.e. a protease or growth factor, for example). Claim 6 has been interpreted as referring to a length of 3 to 15 amino acids. The term 'substantially' has been given the broadest reasonable interpretation such that any blockage or partial blockage is substantial.

This is a provisional obviousness-type double patenting rejection.

Claims 1-6,13-16,18-19,22 are directed to an invention not patentably distinct from claims 1-4,7-16 of commonly assigned 12/041,955 as discussed above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 12/041,955, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Prior art of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Sojomihardjo et al (WO 96/40829 as cited previously) teach (claim 18 page 53) an article comprising a crosslinked polypeptide (i.e. a matrix comprising polymers – polypeptides are polymers) having a biologically active material (i.e. therapeutic agent) entrapped therein. Sojomihardjo teach the compositions as wound dressings (abstract last sentence, claim 6).

Woerly et al. (Biomaterials (2001 v22 pages 1095-1111 as cited previously). Woerly teach PHMPA interconnected with specific peptides such as GGRGD (abstract, Figure 1). Any rejection using Woerly would be repetitive of the rejections above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner, Art Unit 1654

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